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Précis: Autophagy promotes cell survival and tumorigenesis in a model of hereditary breast cancer driven by conditional knockout of Poib2 in the mammary gland.

Pten-Null Tumors Cohabiting the Same Lung Display Differential AKT Activation and Sensitivity to Dietary Restriction ....................... 908
Précis: Heterogeneous AKT activation in Pten-null murine lung tumors and PTEN-deficient human NSCLCcs suggests that PTEN loss does not always correlate with AKT activity.

Stromal EGF and IGF-I Together Modulate Plasticity of Disseminated Triple-Negative Breast Tumors ......... 922
Précis: Expression of EGF and IGF-I in the tumor microenvironment is required for malignant conversion of certain indolent cancer cells and accelerates recurrence of triple-negative breast cancer.

TGF-β Signaling in Myeloid Cells Is Required for Tumor Metastasis. ......... 936
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- Early Results Promising for LDK378 in ALK-positive NSCLC
- BRAF and MEK Inhibitors Approved for Melanoma
- Many Patent Protections Remain After Supreme Court Ruling
- Putting a Value on the Human Genome Project
- J&J Buys Aragon for Prostate Cancer Drug
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ON THE COVER
Curry and colleagues made the surprising observation that two adjacent tumor types with either low or high AKT activity can develop in Pten-null lungs. Heterogeneous AKT activation was cell autonomous and associated with differential expression of ectonucleoside triphosphate diphosphohydrolase 5 (ENTPD5), a UDPase that promotes receptor tyrosine kinase folding in the endoplasmic reticulum. Knockdown of ENTPD5 led to a reduction in levels of insulin growth factor receptor β (IGFIRβ), an upstream activator of AKT. In human non–small cell lung cancers (NSCLC), AKT phosphorylation was directly correlated with ENTPD5 expression, but not always with loss of PTEN expression. Together, these findings suggest that PTEN loss may not be sufficient to activate AKT and may not be an appropriate biomarker of PI3K/AKT activation or response to PI3K/AKT-targeted therapies. For details, please see the article by Curry and colleagues on page 908.